[redacted]

FACILITY FORM 602

N67 12971 (ACCESSION NUMBER)	(THRU)
48 (PAGES)	1 (CODE)
CR 80337 (NASA CR OR TMX OR AD NUMBER)	04 (CATEGORY)

EXOTECH
INCORPORATED

GPO PRICE $ ______

CFSTI PRICE(S) $ ______

Hard copy (HC) 2.00

Microfiche (MF) .50

ff 653 July 65

525 SCHOOL STREET, S. W. • WASHINGTON, D. C. 20024

ANALYTICAL TECHNIQUES IN PLANETARY QUARANTINE AND SPACECRAFT STERILIZATION

Final Report

Contract NASw-1340
for
National Aeronautics and Space Administration
Office of Biosciences

Prepared by: Saul Schalkowsky
Samuel Schalkowsky
Principal Investigator

Approved by: W. C. Cooley by D. L. Fain
William C. Cooley
Program Manager

November 1966

EXOTECH INCORPORATED
525 School Street, S.W.
Washington, D. C.

ABSTRACT

Analytical methods and calculations are reported which relate to

(1) the prediction of the hazard of biological contamination of other planets

(2) the specification of planetary quarantine requirements

(3) the functional correlation of experimental data on microbial lethality during heat sterilization, and

(4) the proper allowance for integrated lethality during transient heat-up and cool-down of a space capsule.

Existing analytical techniques in the field of sterilization are found to be inadequate for the planetary quarantine program and improved methods have therefore been developed in all of the areas considered. These are summarized in the report and related documentation.

TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

1. INTRODUCTION

This is the final report under contract NASw-1340, carried out by Exotech, Incorporated for the NASA Headquarters, Office of Biosciences. The scope of this contract was originally confined to the conduct of a six month study of analytical techniques in dry-heat sterilization of planetary spacecraft and work on this effort began October 13, 1965. However, effective June 1, 1966, the original contract scope was increased to include the development of analytical techniques needed to derive planetary quarantine requirements and the completion date of the contract was extended to November 13, 1966. This report covers the entire thirteen (13) month program and summarizes results for heat-sterilization aspects as well as the planetary quarantine requirements part of the study.

This report is divided into two parts. The first part deals with analytical techniques in the formulation of planetary quarantine requirements and is covered in Section 2 below. The second part concentrates on the implementation aspects of the heat sterilization requirement and is covered in Section 3. Since in the present work these two areas are independent from an analytical point of view, i.e. the heat sterilization requirement stems from one parameter in the formulation of planetary quarantine requirements, the two sections contain separate conclusions and recommendations.

Work performed under the subject contract paralleled an evolutionary process at NASA both with regard to the rationale underlying planetary quarantine requirements as well as the issuance of numerical magnitudes for the guidance of engineering development efforts. To make best use of the Exotech studies under this contract it proved desirable to publish results as they became available, rather than defer their publication to the issuance of this final report. Another consideration which encouraged the provision of separate topical reports is that some of the subjects treated are of greater interest either to the biological community associated with spacecraft sterilization or to the engineers dealing with this problem, but not to both.

In view of the above considerations, the approach taken in preparing this report was as follows. Reports which had previously been issued and are readily available through NASA documentation sources, e.g. STAR, are referenced but are not included in this report. Reports which had been issued earlier but are not as yet available from other sources are separately submitted with this report. All of the above reports are, however, also discussed in the text of this report to relate their subject matter to the overall study and to summarize their major conclusions. Table I provides an index to all the topics covered in the study, listing reports dealing with each topic and the sources from which they are available.

Dr. William C. Cooley was Program Manager of this study and also contributed in the areas of (1) heat transfer analysis relating to the integration of lethality during thermal transients and (2) the development of analytical techniques in the formulation of planetary quarantine requirements. Samuel Schalkowsky was the principal investigator. He was assisted by Dr. Robert Wiederkehr of Westat Research, Inc. in the area of theoretical statistics. Additional support was utilized from Matthew Barrett and other staff personnel of Exotech, Incorporated.

TABLE I

Index to Topics Studied and Reports Issued Under Contract

NASw-1340 by Exotech, Incorporated

Final Report Section	TOPICAL REPORTS			
	Title	Date	Exotech Identification	Source
2. Definition of Planetary Quarantine Requirements	A Critique of Current Spacecraft Sterilization Standards	January 3 1966	--	STAR - Accession No. N66-23753
	Analysis of Planetary Quarantine Requirements	April 15 1966	--	STAR - Accession No. N66-27531
	Estimation of Planetary Contamination Probabilities due to the Flight of the U.S.S.R. Venus 3	August 10 1966	--	Separately submitted to NASA with this Final Report
3. A. Stochastic Model for Sterility Testing and Prediction	A Stochastic Sterilization Model	May 6 1966	TR-13	STAR - Accession No. N66-27536
3.B. Survival Probabilities in Heat Sterilization	Log-Normal Model for Microbial Survival in Heat Sterilization	October 1966	TR-015	Separately submitted to NASA with this Final Report
3. C. Significance of Thermal Transients in Heat Sterilization	This topic is covered in the Final Report, including Appendices A, B and C thereto.			

2. DEFINITION OF PLANETARY QUARANTINE REQUIREMENTS

During the first part of this study a review was made of existing analytical procedures for the definition of planetary quarantine requirements. These were found to be deficient for the evolving needs of the program and a paper was prepared defining shortcomings and proposed direction of change. This paper, titled "A Critique of Current Spacecraft Sterilization Standards", by S. Schalkowsky (dated January 3, 1966), is available from STAR through accession number N66-23753.

To meet existing needs of the program, a simple but adequate analytical framework was formulated, defining the relationship between planetary quarantine requirements and estimated probabilities of planet contamination. Emphasis was placed on the form in which the requirements are stated so as not to constrain their implementation unnecessarily. A document summarizing this analytical model was prepared by S. Schalkowsky and W. C. Cooley under the title "Analysis of Planetary Quarantine Requirements", (dated April 5, 1966) and is available through STAR under accession number N66-27531. This document contains numerical values for the quarantine requirements, based on the assumed set of values for the various "judgment factors" entering into the model. However, alternate sets of requirements are also provided to show the relative significance of the judgment factors.

In the course of the program, an interest developed in the flight of the U.S.S.R. Venus 3 spacecraft and its impact on the planet. Specifically, there has been (and still is) speculation that Venus might already be contaminated because of this event. An analysis was therefore made to assess the impact of the Venus 3 flight on quarantine requirements for future flights to that planet. This analysis is summarized in the document titled "Estimation of Planetary Contamination Probabilities due to the Flight of the U.S.S.R. Venus 3", dated August 10, 1966, which is being separately submitted to NASA.

Much of the discussion on planetary quarantine requirement is carried out through the COSPAR Consultative Group on the Harmful Effects of Space Experiments and involves participation by representatives from the U.S.S.R. and other interested nations. Some of the work described in this section was thus oriented to support NASA's efforts in these discussions. In this category also belong the recommendations provided by Exotech for a standardized nomenclature in the analysis of planetary quarantine, which are included below.

In addition to the results contained in the documents previously published, the following recommendations are provided:

A. Recommended Nomenclature for Planetary Quarantine Analysis

The following symbols for quantitative parameters, events and the probabilities of the occurrence of these events is recommended for use in the formulation of planetary quarantine standards and analyses aimed at demonstrating adherence to these standards:

P_c - probability that the planet under consideration will be contaminated during a specified time period of unmanned exploration.

$P_c(M)$, $P_c(V)$ - probability values of P_c referring specifically to Mars and Venus, respectively.

n - estimated number of sterilized lander vehicles launched during the time-period under consideration which reach the planet surface.

n' - estimated number of unsterilized buses, orbiters and flybys launched over the time period under consideration.

$P(n_j)$ - probability that any one sterilized lander, i.e. the j-th one, will cause planetary contamination.

$P(n'_j)$ - average probability that any one bus, orbiter or flyby, i.e. the j-th one, will cause planetary contamination.

N - number of viable organisms in a sterilized lander upon arrival at the vicinity of the planet.

N_o - number of viable, heat resistant organisms on and in a lander prior to sterilization.

$P(N \leq 1)$ - probability that N is less or equal to one.

N' - estimated number of viable organisms on an unsterilized spacecraft or in ejecta from the spacecraft upon arrival in the vicinity of the planet, i.e. at the time when they become a contamination hazard.

N'_o - number of viable organisms on a bus, orbiter or flyby at launch.

$E(N')$ - expected number of viable organisms released on the planet surface or into its atmosphere from an unsterilized spacecraft or parts thereof.

event r - release of viable organisms from a sterilized lander on the planet surface or into its atmosphere.

$P(r)$ - average probability that r will occur.

event r' - release of viable organisms from an unsterilized bus, orbiter, flyby or parts thereof on the planet surface or its atmosphere.

$P(r')$ - average probability that r' will occur. (This probability will be a function of N'.)

event g - growth and spreading initiated by viable organisms from a sterilized vehicle, leading to planetary contamination.

$P(g)$ - average probability that g will occur.

event g' - growth and spreading initiated by viable organisms from unsterilized spacecraft or portions thereof, leading to planetary contamination.

$P(g')$ - average probability that g' will occur. (This probability may be defined as a function of $E(N')$).

a' - arrival of unsterilized spacecraft or portions thereof in the vicinity of the planet so as to permit the release of unsterilized organisms on the planet surface or into its atmosphere. a' also includes the arrival of organisms from the unsterilized spacecraft aboard the sterilized lander because of recontamination.

P(a') - average probability that a' will occur. (Note: since the landing vehicles being considered are only those which will reach the planet, a definition for P(a), i.e. the probability that it will land, is superfluous.)

subscript i = 1, 2, 3....denotes the various sources of contamination due to unsterilized vehicles or parts thereof.

t - total sterilization time.

D - the time required to reduce a heat resistant biological population, N_0, (of a single species) by one decade at a constant temperature.

B. Recommended Analytical Basis for Planetary Quarantine

It is recommended that, for the present, planetary quarantine standards be established on the basis of the following (for symbol definitions, reference is made to the Proposed Standard Nomenclature):

(a) Average values of $P(n_j)$ and $P(n_j')$ will be used over the estimated period of unmanned exploration, i.e. $P(n_j)$ and $P(n_j')$ will be taken to be the same for each of the missions considered.

(b) The total probability P_c will be computed from

$$P_c = n\,P(nj) + n'\,P(nj') \qquad (1)$$

(The additional term $(-\,nP(n_j)\,n'P(n'_j))$ required by statistical theory is neglected since $P(n_j)$ and $P(n_j')$ will be much smaller than unity. Doing so will also make the resulting P_c more conservative.)

(c) Events N, r and g are taken to be stochastically independent and $P(n_j)$ defined as

$$P(n_j) = P(N<1)\,P(r)\,P(g) \qquad (2)$$

(d) Events a', r', g' are taken to be stochastically independent and $P(n'_j)$ defined as

$$P(n'_j) = \sum^{i} \left[P(a')\,P(r')\,P(g')\right]_i \qquad (3)$$

It is noted that the estimation of $P(r')_i$ will be a function of N'_i. It is also recommended that bounds be placed on the value of $P(g')$ and the choice of $P(g')_i$, i.e. the probability of growth and spreading for a particular contamination hazard be made a function of $E(N')_i$.

C. Recommended Future Studies

(a) Enlarge the present simplified analytical model by introducing a time dependence for mission requirements, i.e. allow for different requirements for the various missions. Doing this will allow for improved accuracy in predicting the contamination hazard and improvements in the state of the art of sterilization technology as the program progresses.

(b) Develop a methodology for demonstrating compliance with planetary requirements prior to flight when only analytical, rather than experimental means are available for this purpose. This methodology must encompass all of the sources of accidental contamination which are considered in planning sterilization aspects of the mission.

3. IMPLEMENTATION OF QUARANTINE REQUIREMENTS

In heat sterilization of a spacecraft, the particular requirement to be implemented is the probability of a viable organism remaining in the spacecraft at the conclusion of the heat cycle. This requirement relates to $P(N \leq 1)$, defined in the preceding section, which includes the additional probability of survival of the heated, but viable, organism during flight to the planet.

Analytical techniques relating to the implementation of the heat sterilization requirement can be divided into three categories. The first category deals with the general statistical aspects of the problem, identifies the various problem areas and defines their interrelation. This area of work is described below in Section A. The second category relates to the choice of a suitable function for the probability of survival in heat sterilization and is described in Section B. Finally, the significance of thermal transients during sterilization is discussed in Section C.

A. Stochastic Model for Sterility Testing and Prediction

One area which was found to require clarification and modification deals with the analytical model which relates experimental data on microbial heat resistance to the extrapolation of these data to operational requirements. Current difficulties arise not from the absence of an analytical model but rather from the fact that the model being used is based upon unproved hypotheses and there is ever increasing evidence that these hypotheses may be wrong. Specifically, it is currently accepted as a "law" that microorganisms exposed to a heat environment lose viability exponentially, i.e. the number of survivors is decreased by one decade in constant intervals of heating time. The validity of this "law" has been questioned ever since it was promulgated and was also scrutinized in the study under the present contract (see Section B below). However, of interest here is the fact that current analytical models in sterilization are predicated upon the validity of the exponential "law". But this is quite unnecessary since the model can also be formulated without constraints on the specific form of the survival function. Thus, the relationship between experimental test parameters and probabilities of sterility (or contamination) of a spacecraft can be evolved on the basis of an undefined survival function. Clearly, such a formulation would be preferred since it is free of any questions concerning the validity of a particular survival function, and can facilitate the study of alternate survival functions. Such a model has been evolved and is described in the Exotech Report TR-13 titled "A Stochastic Sterilization Model" and dated May 6, 1966. It is available from STAR under accession No. N66-27536.

The principal use of the stochastic model, as of any other analytical model, is to provide a framework for specific, problem-oriented investigations. One such application has been the study of survival-probability functions in heat sterilization which is described in Section B below. The report itself considers two additional applications. One of them deals with alternate experimental procedures, i.e. the counting of survivors vs. the sterility end-point test, and it is concluded that when the initial viable population N_0 is known to a high degree of accuracy, the two procedures give similar precision in defining parameters of the time-survivor curve. The case where N_0 is not accurately known has not as yet been evaluated.

The second application of the model deals with the extrapolation of survivor counts, as obtained experimentally over a small number of decades in population reduction, to low probabilities of contamination, using an analytical extension of the survivor curve. It was found that (1) such an extrapolation is valid for probabilities of contamination of 10^{-2} or less, provided the analytical representation of the time-survivor curve is valid and (2) it is immaterial, from a practical point of view, whether the probability of contamination is specified in terms of the probability of exactly one survivor, or the probability of one or more survivors.

B. Survival Probability in Heat Sterilization

As noted in the preceding section, the logarithmic (D-value) model for microbial population reduction is the generally accepted basis for sterility prediction and for the formulation of process requirements. However, experimental data has frequently contradicted this model, and in the data generated in connection with planetary quarantine requirements, the conflict has been too glaring to be overlooked. This program has therefore included a detailed study of alternate models for relating population reduction to sterilization time.

For a particular sterilization time, t, the population reduction expressed as the ratio of viable organisms $N(t)$ to the initial viable population N_0 is a measure of the probability that anyone organism will survive the heating time t. This probability is denoted as $P_s(t)$ and the complementary probability of death $P_d(t)$ is then

$$P_d(t) = 1 - P_s(t) \qquad (3\text{-}1)$$

In the logarithmic model, the time variation of the survival probability takes on the form

$$P_s(t) = 10^{-t/D} \qquad (3\text{-}2)$$

which is applicable at constant temperature.

In the present study, a variety of alternate functional forms were considered for $P_s(t)$ in an attempt to obtain a better fit to experimental data than is provided by the logarithmic model of equation 3-2. The form which received the most detailed attention is the log-normal distribution for $P_d(t)$, i.e. where the probability of deaths in the interval of time t is normally distributed as a function of the logarithm of t. The analytical basis of this model was defined and the relationship between its variables and the experimental parameters was identified. The analytical model was then studied in relation to existing experimental data and its utility was assessed. The above work is summarized in Exotech Report TR-015 by S. Schalkowsky and R. Wiederkehr titled "Log-Normal Model for Microbial Survival in Heat Sterilization" and which is being separately submitted to NASA. Its principal conclusions may be summarized as follow:

(1) The log-normal model fits a wide variety of experimental conditions beyond an initial heating phase in which two to three decades of population reduction occurs. The degree of deviation during this initial die-off phase depends upon the medium in which the organisms are contained. This deviation has been found to have consistent characteristics and is therefore itself of interest as a measure of the influence of the medium on rate of die-off.

(2) The log-normal model would require longer-heating times than the logarithmic model when both are derived from data which is essentially linear on a semi-log plot of N/N_0 vs. time. Such linear plots are, however, only found for a small number of decades in population reduction. For more extensive data, the logarithmic model cannot realistically be applied, whereas the log-normal model gives a more accurate fit to the experimental data and provides a more realistic and conservative basis for defining sterilization requirements.

C. Significance of Thermal Transients in Heat Sterilization

Although the determination of microbial resistance to heat sterilization is most conveniently done in the laboratory using a constant temperature environment, actual sterilization processes must allow for thermal transients during heat-up and cool-down of the items being sterilized. This has long been recognized in the food industry and standard procedures are in use to account for the lethality during the thermal transients.

(See references 3, 4 and 5.) The reason for doing this is, of course, to minimize the destructive effects of heat sterilization on the product by limiting the process to no more than that needed to achieve the desired level of sterility assurance. In the case of spacecraft sterilization there is a similar consideration, since heat is either known or can be expected to degrade equipment performance and/or reliability, and excess heating, beyond that needed to achieve a specified sterility assurance, is undesirable. Yet, sterilization requirements to date have been specified in terms of time at a fixed temperature without any allowance for the lethality inherent in a range of temperatures below that specified. The effect of such specifications is detrimental to the equipment not only because the spacecraft is subjected to the additional heating during the thermal transients but also because the heat-up time has been viewed as extending to that point in time when the innermost component has reached the specified sterilization temperature. The formal heat cycle would start at this time, but in the meanwhile, all but the innermost components have already been at, or near, the sterilization temperature for varying lengths of time.

To assess the significance of thermal transients in spacecraft sterilization, calculations were performed of the sterilization which was accumulated during heat-up and cool-down of small capsules in the thermal tests by the General Electric Co. (Reference 1). Since planned missions to Mars may include large landing vehicles, additional analysis was performed aimed at extrapolating the calculated results to these larger vehicles. A summary of the analysis and its results is provided below.

Assumed Survival Probability Model. - Since this work was performed concurrently with the study of alternate survival probability functions (section IIIB above), it was necessary to use the existing logarithmic model for the analysis of sterilization during thermal transients. In view of the conclusions reached concerning the inadequacy of the logarithmic model, results to be presented here must therefore be viewed as qualitative, i.e. a valid quantitative evaluation remains to be performed on the basis of the log-normal model or suitable modifications thereof.

For the present, it is assumed that the sterilization requirement can be specified in terms of the required ratio of reduction, R, in the viable microbial population,

$$R = \frac{N_o}{N} \tag{3-3}$$

where N_o is the initial viable population, at $t = 0$, and N is equivalent to the probability of one survivor at time t (see Section 3 A) if N is much less than unity. In accordance with the logarithmic model,

$$\frac{1}{R} = \frac{N}{N_o} = 10^{-t/D} \tag{3-4}$$

and taking logarithms to the base 10,

$$-\log_{10}R = -\frac{t}{D} = \eta \tag{3-5}$$

In differential form, equation (3-5) becomes

$$d\eta = -\frac{1}{D}\,dt \tag{3-6}$$

R or η represent the sterilization requirement. Thus in the calculations to be described herein, R was taken as 12, i.e. requiring 12 decades of reduction in N_o. Since for our present purposes the D-value is a function of temperature, sterilization must be expressed in integral form using equation (3-6):

$$\int_{t_1}^{t_s} \eta = \eta_2 - \eta_1 = \log \frac{R_1}{R_2} = -\int \frac{dt}{D(T)} \tag{3-7}$$

where D(T) denotes the temperature dependence of D.

<u>D-Value Temperature Dependence Function</u>. - Figure 1 shows the D-values which had been specified by NASA (Reference 6) at the time these calculations were performed. A number of approaches are possible in fitting

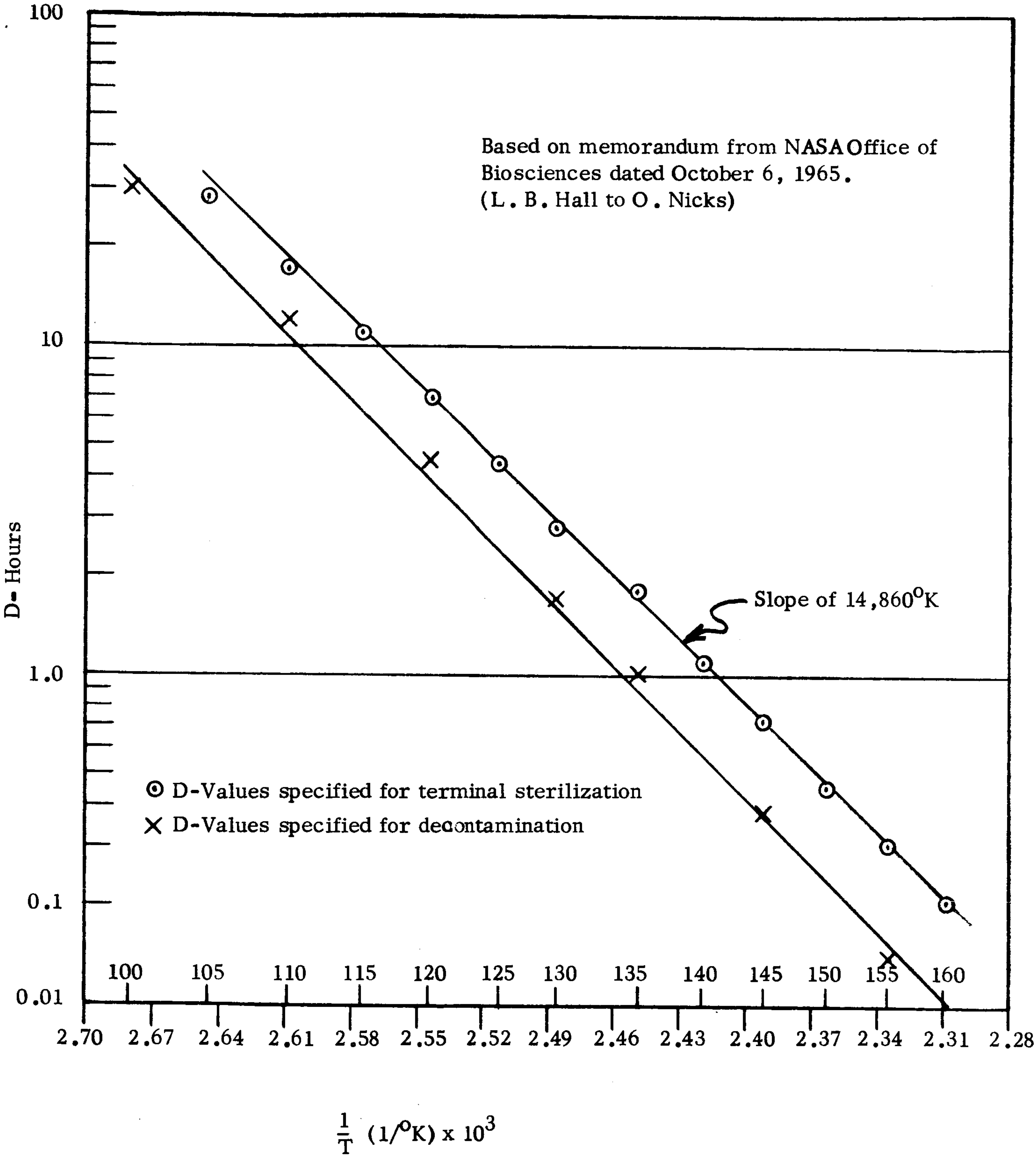


Figure 1 - Alternate Dry-Heat Sterilization D-Values

a functional relationship to this plot. One approach is to use the Z-value concept which, essentially, assumes the linear relationship

$$\log_{10} D = K_1 - K_2 T \tag{3-8}$$

where K_1, K_2 are constants.

This is a common basis in food sterilization and it has also recently been used by the General Electric Co. to make calculations in spacecraft sterilization (see Reference 2). This relationship has also been assumed in Appendix C. However, it has been shown in the literature, e.g. references, 3, 4, 5 and others, that the Z-value gives erroneous results when the range of temperatures is sufficiently large, e.g. 50°C or more, and that the Arrhenius form of temperature dependence is more accurate. We have therefore used the Arrhenius relationship in making calculations over the temperature range from 105°C to 150°C. This relationship takes the form

$$\frac{1}{D} = A e^{-T_a/T} \tag{3-9}$$

where T_a - activation temperature constant

T - temperature in degrees absolute

A - a constant for a given bacterial species

T_a is frequently shown as E/R, where E is referred to as the activation energy and R is the gas constant. The particular value of T_a used here is obtained from the slope of Figure 1 and a value of

$$T_a = 14{,}860^\circ K$$

has been found to produce a good fit for the data shown in Figure 1.

Combining 3-7 and 3-9,

$$\Delta \eta = \eta_1 - \eta_2 = \log \frac{R_2}{R_1} = A \int_{t_1}^{t_2} e^{-T_a/T} \, dt \tag{3-10}$$

Results of Calculations on Small Spacecraft Configurations. - To integrate equation 3-10 it is necessary to define the variation of temperature with time. Although for a particular spacecraft configuration such a functional relationship could be fitted to the temperature test data (as will be done below) a more general approach is to use piece-wise linear integrations, i.e. choose consecutive small intervals of time in which a linear change of temperature with time will be a sufficiently accurate approximation. The procedure for evaluating the integral of 3-10 in this manner is described in Appendix A. This method was applied to test data by the General Electric Company (Reference 1) on capsules weighing about 200 lbs. with various component densities and heated either with or without a canister around the capsule. These combinations produce a variety of temperature profiles throughout the capsule during heat-up and cool-down and afford an opportunity to assess the varying degrees of sterilization which are achieved during the temperature transients.

Table II summarizes the calculations using the G.E. test data and Figures 2, 3 and 4 show both the temperature profiles measured by G.E. and the corresponding accumulation of sterilization for each of these cases evaluated. As noted in these figures, the cumulative sterilization is expressed as a percentage of the required 12 D-values of population reductions. Thus a cumulative sterilization value of 150% represents a reduction of 18 decades, as compared to the required 12 decades of reduction.

The significance of the heat-up and cool-down periods is evident from the data summarized in Table II. Thus, even for these small capsules, a significant part of the sterilization requirement is achieved during the thermal heat-up transient while approaching a uniform temperature of 150°C. Indeed, nearly all of the requirement is accomplished during the transients in case B-3, the full requirement is achieved in case A-2 and an excess of at least 7 decades reduction is obtained in case A-3. (In this last case, if

STERILIZATION DURING CAPSULE HEAT-UP AND COOL-DOWN

Based on thermal test data of a typical 200 lbs. capsule by the General Electric Company (Final Report under Contract NAS8-11372), Ref. 1

			HEAT-UP(3)		COOL-DOWN(3)		TOTAL	
G. E. Code	Description	Location	Sterilization(1)	$t_{105-150}$ (2)	Sterilization(1)	$t_{150-105}$ (2)	Sterilization (1)	$t_{105-105}$ (2)
B-3	With canister;	Heat shield maximum	75%	12 hrs.	11%	2.5 hrs.	86%	14.5 hrs.
	Low density componentry	Internal structure	66%	12 hrs.	15%	3.1 hrs.	81%	15.1 hrs.
		Coldest component	43%	12 hrs.	41%	4.8 hrs.	84%	16.8 hrs.
A-2	No canister;	Heat shield maximum	102%	12.6 hrs.	11%	2 hrs.	113%	14.6 hrs.
	High-density	Internal structure	82%	12.6 hrs.	23%	3.2 hrs.	105%	15.8 hrs.
		Coldest component	74%	12.6 hrs.	26%	3.6 hrs.	100%	16.2 hrs.
A-3	With canister;	Heat shield maximum	178%	20 hrs.	7%	1.7 hrs.	185%	21.7 hrs.
	High-density	Internal structure	130%	20 hrs.	28%	4.5 hrs.	158%	24.5 hrs.
		Coldest component	127%	20 hrs.	32%	4.9 hrs.	159%	24.9 hrs.

(1) 100% sterilization is equivalent to 12 decades of population reduction.

(2) Time spent in the varying temperature range (°C) noted in the subscript.

(3) The heat-up period is completed when all parts of the capsule reach a temperature within one or two degrees C of the driving temperature, which in all of the G. E. test has been about 150°C. Cool-down, for the purposes of these calculations, starts immediately after completion of the heat-up period, i.e., there is no constant temperature soak period.

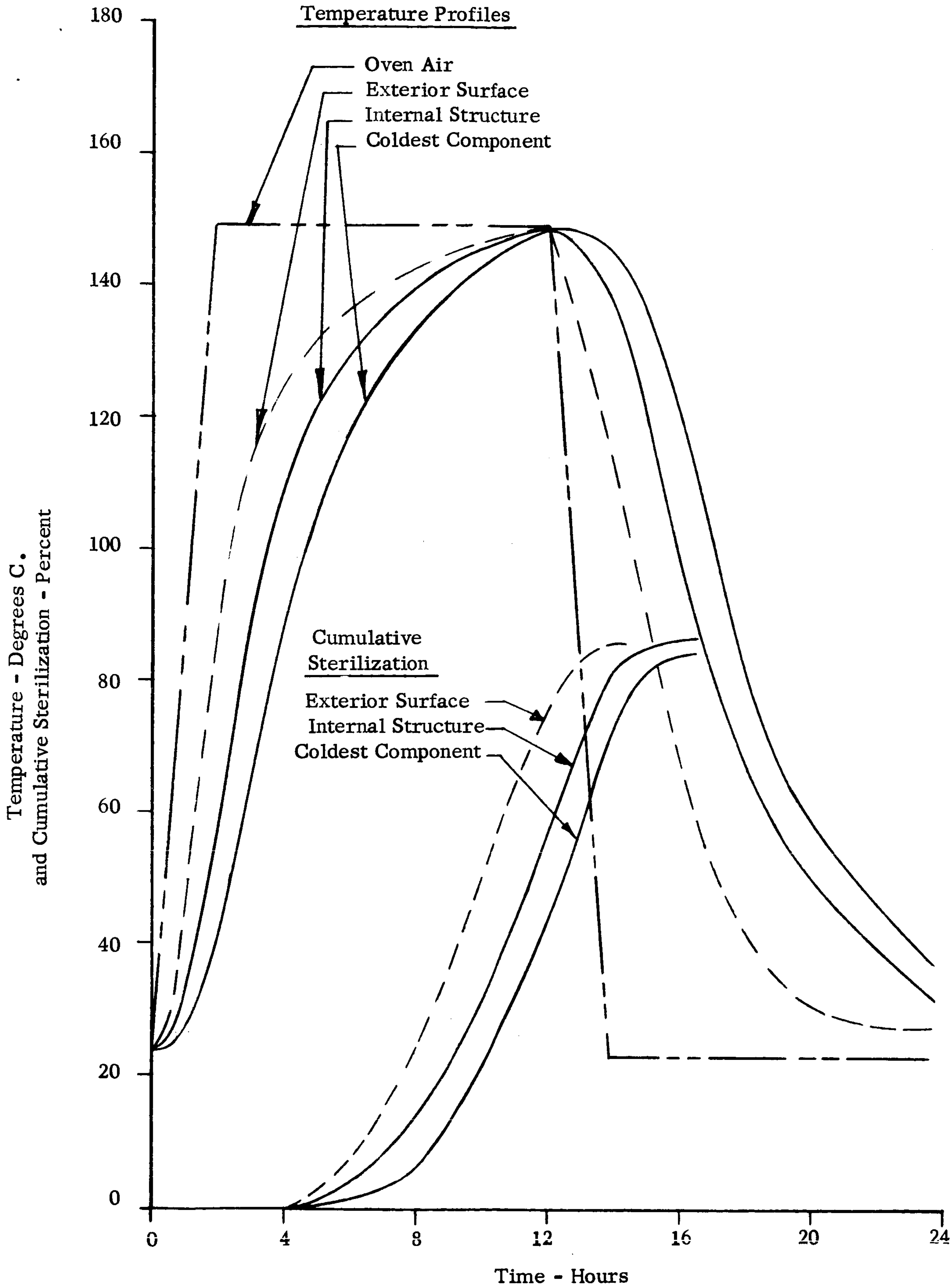


Figure 2. - Results of Integrated Lethality Calculations for Case B-3

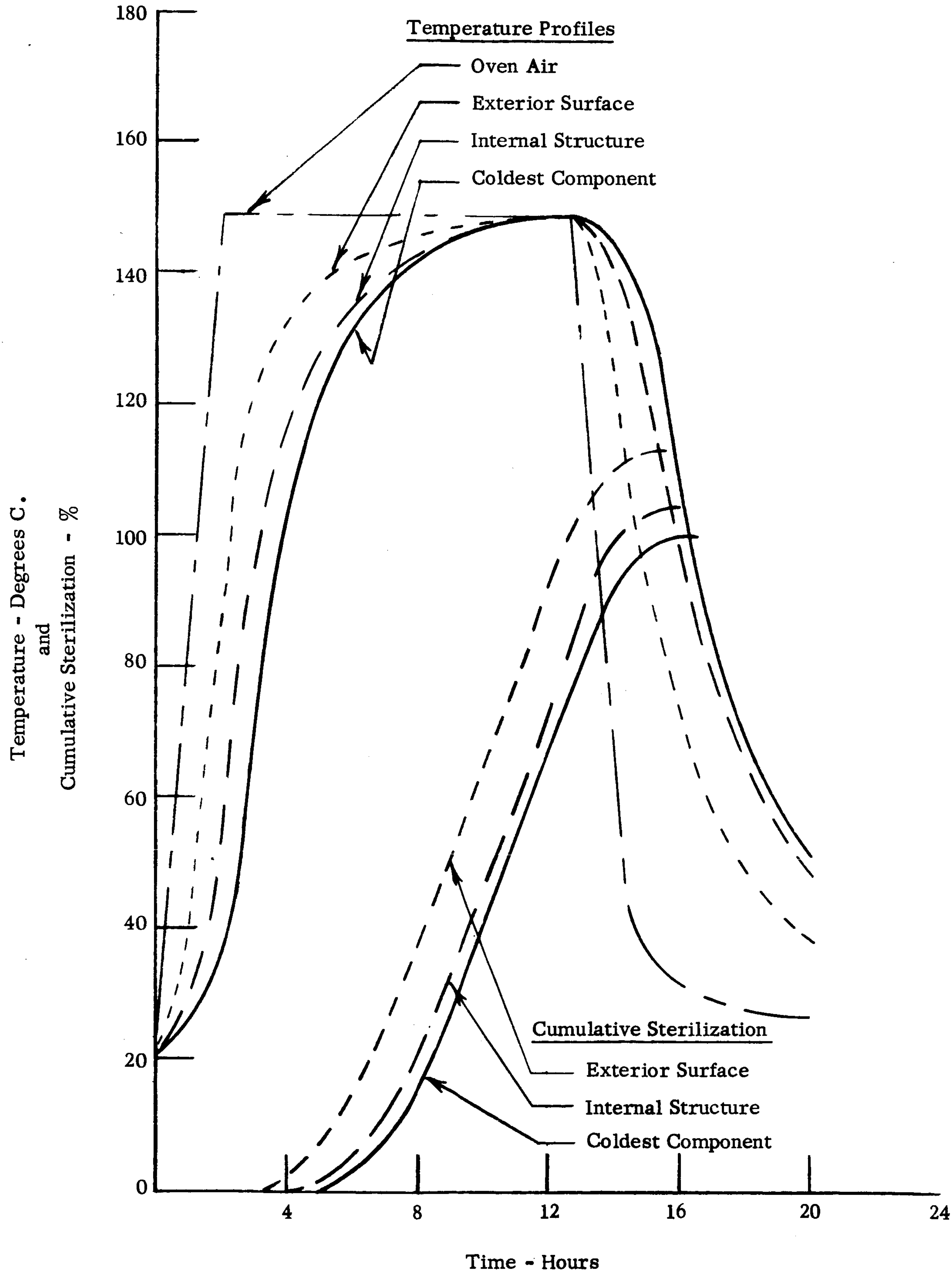


Figure 3 - Results of Integrated Lethality Calculations for Case A-2

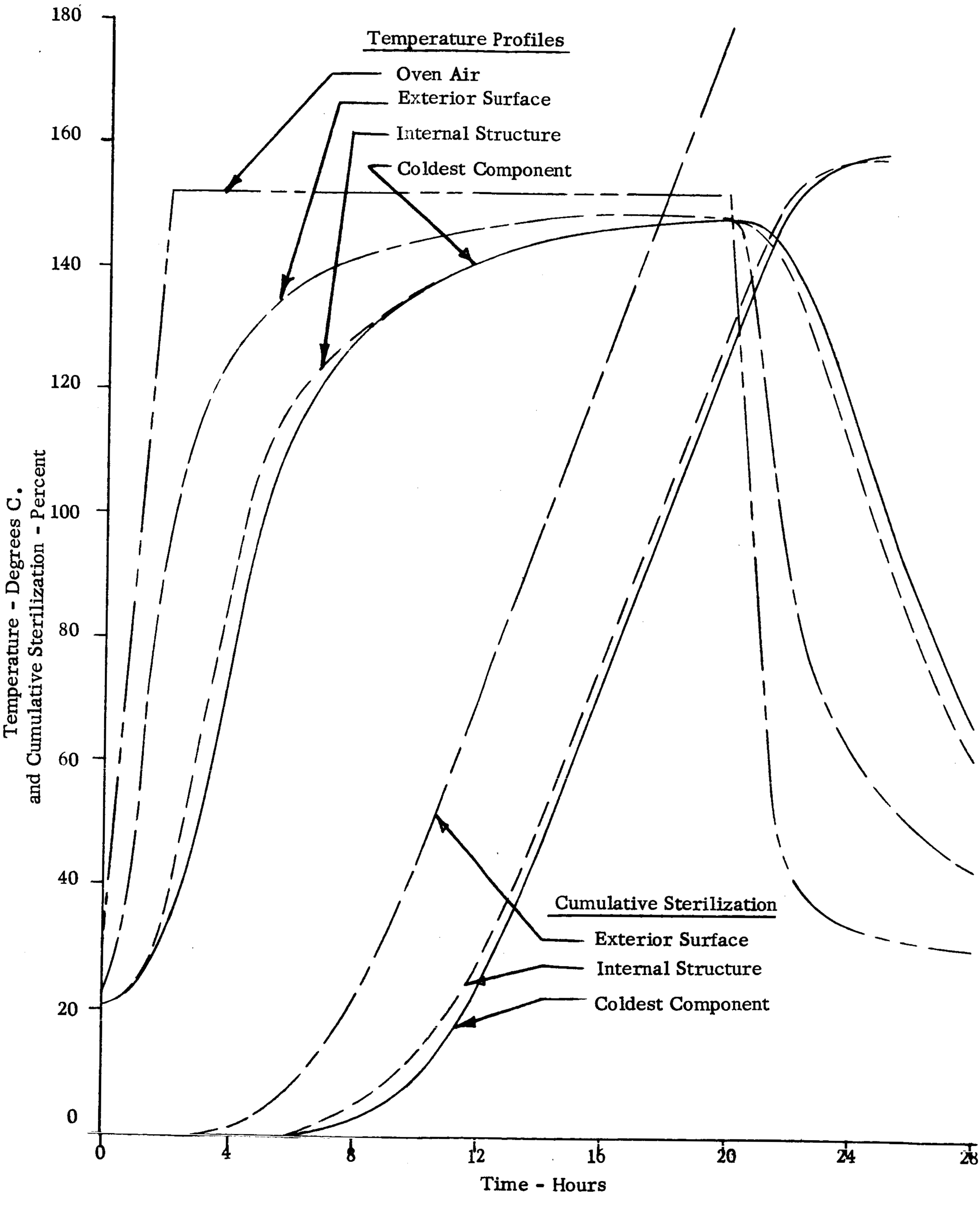


Figure 4. - Results of Integrated Lethality Calculations for Case A-3

if the effect of transients were ignored and a 12 decade reduction were still required at a constant 150°C temperature, the total reduction would be 31 decades. Thus, an initial population of 10^{27} spores, probably more spores than are present on the entire earth, would be sterilized to a probability of 10^{-4} that there will be one survivor.)

Of equal significance is the indication in the data presented herein that the heat-up and cool-down periods serve to equalize the amount of sterilization occurring at various locations in the capsule. Thus, although internal components lag the exterior parts during heat-up and show a correspondingly lower accumulation in integrated lethality, they stay at the high temperature longer during cool-down and "catch-up" with the exterior parts during this phase of the heat transient. The net effect is that there are no major differences between locations in the capsule when both phases of the heat transient are considered.

Extension to Other Spacecraft Configurations. - Future missions including planetary landing vehicles are likely to utilize vehicles on the order of 5 or 10 feet in diameter and weighing 2,000 lbs. or more. Furthermore, a preference has recently been shown for sterilization temperatures lower than the 150°C used in the G.E. tests. It is therefore of interest to assess the significance of heat transients under these conditions.

In the absence of actual temperature data, it is necessary to assume an analytical function for the anticipated temperature variation of the spacecraft during the heat transient. The approach taken here is to obtain an empirical fit to the data available for small capsules and to extrapolate the empirical relationship thus obtained to the larger spacecraft. This is done in Appendix B, assuming the capsule to be a homogeneous sphere subject to a step change in furnace temperature. The result is an approximately exponential function for central temperature variation with time during the heat-up period. A plot of this function with assumed values of thermal conductivity, thermal diffusivity and surface heat transfer coefficients is shown in Figure B-1 of Appendix B indicating a reasonably good approximation to the test data in the temperature range of interest, i.e. from 105 to 150°C.

The above heat transfer analysis provides a means for estimating the heat-up times which would be encountered in the larger vehicles if a uniform temperature were required throughout. As shown in the sample calculation of Appendix B, a 10 foot diameter sphere would require on the order of 580 hours, i.e. about 20 days, before its center would reach 149°C when exposed to a constant 150°C oven temperature. This gives some indication of the procedural implication of the constant temperature requirement, independent of the equipment degradation aspects which have previously been noted. It shows that means should be actively sought for heating large capsules more rapidly.

The heat transfer analysis of Appendix B was also used to evolve a closed form solution of integrated lethality during heat-up when the furnace temperature is on the order of 125°C. It was assumed that a linear relationship exists between the logarithm of the D-value and temperature in the range $105^{\circ}C < T < 125^{\circ}C$ with sufficient accuracy for estimation purposes. Results of this analysis are summarized in Figure C-1 of Appendix C and it is seen that even with the lower oven temperature of 125°C, the required 12 decades of reduction would be achieved during heat-up alone of an 8.8 foot diameter sphere (without a canister).

Conclusions. - The formulation of heat sterilization requirements on the basis of a constant temperature, uniformly achieved throughout the spacecraft, is not an appropriate means for achieving a safety factor in sterility assurance. For it produces an excess in sterility assurance which, in terms of the viable population destroyed, is quite unrealistic and it obtains this excess at the expense of equipment reliability. Since equipment reliability magnitudes needed for planetary exploration are so high as to be essentially unverifiable by direct testing, large safety factors in sterility assurance should preferably be obtained by other means.

The heat sterilization requirement should be formulated in integral form, applicable above a specified minimum temperature. Such a formulation will permit a wider latitude in engineering procedures for heating the spacecraft, leading to a better balance between sterility assurance and engineering considerations which are essential to successful accomplishment of flight missions.

D. Recommended Future Studies

In the study of analytical techniques in heat sterilization reported herein, the approach has been to isolate specific areas for independent evaluation. Further work is needed in all of these areas. However, it is believed that there is also a pressing need for a unification of the improved analytical techniques so as to make them available for effective use in the planetary quarantine program. The recommended efforts outlined below would therefore stress those improvemcnts in individual areas which contribute most to the evolution of a unified and consistent analytical basis for planetary quarantine.

(a) Utilize and extend the stochastic model of Section III A to develop test procedures in laboratory evaluations of microbial resistance which are best suited for the definition of sterilization requirements.

(b) Modify the log-normal model of survival probabilities in heat sterilization to a ccount for the accelerated die-off during initial heating.

(c) Establish the temperature dependence of survival function parameters and develop procedures for applying the modified log-normal model to sterilization during thermal transients.

(d) Develop procedures for the selection of time varying oven temperatures in spacecraft sterilization such that sterility requirements will be met uniformly throughout the spacecraft and its components maintained within a selected temperature range.

The efforts described above will be greatly facilitated by complementary biological laboratory tests which are planned consistently with the objectives of the analytical efforts. The determination of temperature dependence of microbial resistance requires additional laboratory tests to provide accurate data over the requisite range of temperatures before analytical techniques can be substantially improved.

4. REFERENCES

1. General Electric Co., Valley Forge, Pa., Final Report under Phase I of contract NAS 8-11372, "Design Criteria for Typical Mars Langing Capsules Requiring Sterilization", December 15, 1965.
2. General Electric Co., Valley Forge, Pa., Third Quarterly Report under Phase III of contract No. NAS 8-11372, "Design Criteria for Typical Mars Landing Capsules Requiring Sterilization", October 1, 1966, G.E. Document No. 66SD4510.
3. Wang, D.I-C., Scharer, J., and Humphrey, A.E., Applied Microbiology, 12, No. 5, p. 451-454, Sept. 1964.
4. Deindorfer, F.H. Appl. Microbiol., 1957, 5, 221.
5. Deindorfer, F.H. and Humphrey, A.E., Appl. Microbiol., 1959, 7, 256.
6. NASA Memorandum from L.B. Hall, Office of Biosciences, to O. Nicks, dated October 6, 1966.
7. Etherington, H., Nuclear Engineering Handbook, McGraw Hill, 1958, p. 1-120.
8. Jakob, M., Heat Transfer, Vol. I., John Wiley, 1949.

APPENDIX A

Piece-wise Linear Integration of Sterilization During Temperature Transients

As defined in the text, the assumed relationship between the D-value and temperature is

$$\frac{1}{D} = A\, e^{-T_a/T} \tag{1}$$

where

T_a = activation temperature constant

T = temperature in degrees absolute

A = a constant for a given bacterial species.

The D-value is defined by the equation for exponential reduction of population:

$$N/N_o = 10^{-t/D} \tag{2}$$

where N is the number of viable organisms at time t and N_o the initial number of viable organisms.

Combining equations 1 and 2 and taking logarithms to the base 10,

$$\log_{10} N/N_o = -t \;\; A \;\; e^{-T_a/T} \tag{3}$$

and from equation 2

$$\log_{10} N/N_o = -t/D \tag{4}$$

The logarithm to the base 10 of N/N_o is viewed as the sterilization requirement η, i.e. it is the specified reduction of the initial N_o expressed in decades. Thus,

$$\eta = \log_{10} N/N_o = -t\, A\, e^{-T_a/T} = -\frac{t}{D} \tag{5}$$

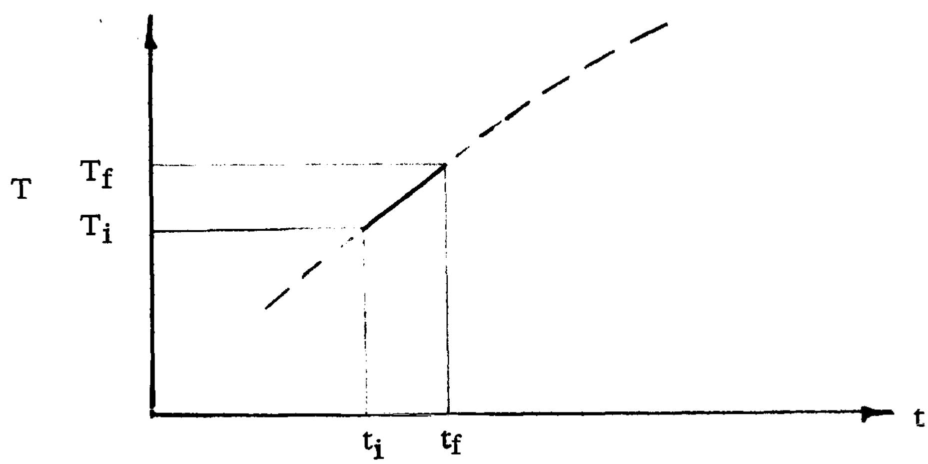
Therefore, η is the required heating time, measured in D-values to accomplish a given reduction factor of the population, N/N_o.

Given η and the D-value for a particular temperature, the required sterilization time, t, can be readily established. Knowing T_a, the parameter which describes the temperature dependence of D, the value of A can also be calculated.

When temperature varies with time, the sterilization requirement can be formulated in integral form based on equation 5. Thus,

$$\eta = - A \int_0^t e^{-T_a/T} \, dt \tag{6}$$

It is assumed that over short intervals of time T varies linearly with time, as sketched below.



The subscript f denotes the final value of T or t in the interval, and i refers to initial values in the interval. If the slope of the line is defined as m, then in this interval

$$T = T_i + m\,(t - t_i) \tag{7}$$

$$t_i \leq t \leq t_f$$

where

$$m = \frac{T_f - T_i}{t_f - t_i} \tag{8}$$

Applying equation 7 to 6,

$$\eta_f - \eta_i = -A \int_{t_i}^{t_f} e^{-T_a/T_i + m(t - t_i)} \, dt \tag{9}$$

To facilitate integration of equation 9, let

$$y = \frac{T_a}{T_i + m(t - t_i)} \tag{10}$$

Then

$$t = \frac{T_a}{my} - \frac{T_i}{m} + t_i \tag{11}$$

and

$$dt = -\frac{T_a}{m} \frac{dy}{y^2} \tag{12}$$

Combining equation 9 with 10 through 12, and writing the integral as a difference between two integrals whose upper limits are infinity,

$$\eta_f - \eta_i = \frac{A\,T_a}{m} \left[\int_{T_a/T_i}^{\infty} \frac{e^{-y}}{y^2} \, dy - \int_{T_a/T_f}^{\infty} \frac{e^{-y}}{y^2} \, dy \right] \tag{13}$$

The above integrals are in the form

$$E_2(x) = \int_x^{\infty} \frac{e^{-y}}{y^2} \, dy \tag{14}$$

For $x < 15$ this integral is obtained from tables, e.g. reference (7). However, for the present calculations

$$x = \frac{T_a}{T} \gg 15 \tag{15}$$

since $T_a = 14{,}860^{\circ}K$ and $T < 600^{\circ}K$. The integral of equation 14 is therefore evaluated from (see reference (7)), the approximate equation:

$$\int_x^{\infty} \frac{e^{-y}}{y^2} \, dy = e^{-x}/x^2 \tag{16}$$

Substituting equations 16 and 15 into 13 and replacing m by equation 7,

$$\eta_f - \eta_i = -\frac{A}{T_a} \frac{t_f - t_i}{T_f - T_i} \left[T_f^2 \, e^{-T_a/T_f} - T_i^2 \, e^{-T_a/T_i} \right] \tag{17}$$

The incremental sterilization $\eta_f - \eta_i$ can be expressed in terms of the total requirement η by replacing A in equation 17 using equation 5. Since equation 5 implies a constant temperature process, we denote the corresponding time and temperature as t_c and T_c, respectively. This yields

$$\frac{\eta_f - \eta_i}{\eta} = B \frac{t_f - t_i}{T_f - T_i} \left[f(T_f) - f(T_i) \right] \tag{18}$$

where

$$B = \frac{1}{T_a t_c e^{-T_a/T_c}} \tag{19}$$

$$f(T_i) = T_i^2 \; e^{-T_a/T_i} \tag{20}$$

$$f(T_f) = T_f^2 \; e^{-T_a/T_f} \tag{21}$$

The value of B is constant and is obtained from any value of t_c, the constant-temperature sterilization time, and its corresponding value of T_c.

To facilitate calculation of equations 20 and 21, a plot of f(T) covering the range of temperatures of interest has been prepared and is shown in Figure A-1.

The procedure for piece-wise integration is therefore as follows:

(1) Select a time interval such that the temperature will be varying in it linearly and define the corresponding values of t_f, t_i, T_f and T_i.

(2) Obtain $f(T_i)$ and $f(T_f)$ from the graph of Figure A-1.

(3) Calculate the amount of sterilization which is accumulated during the chosen interval using equation 18.

The cumulative addition of the increments calculated according to the above procedure yields the total amount of sterilization achieved over the period

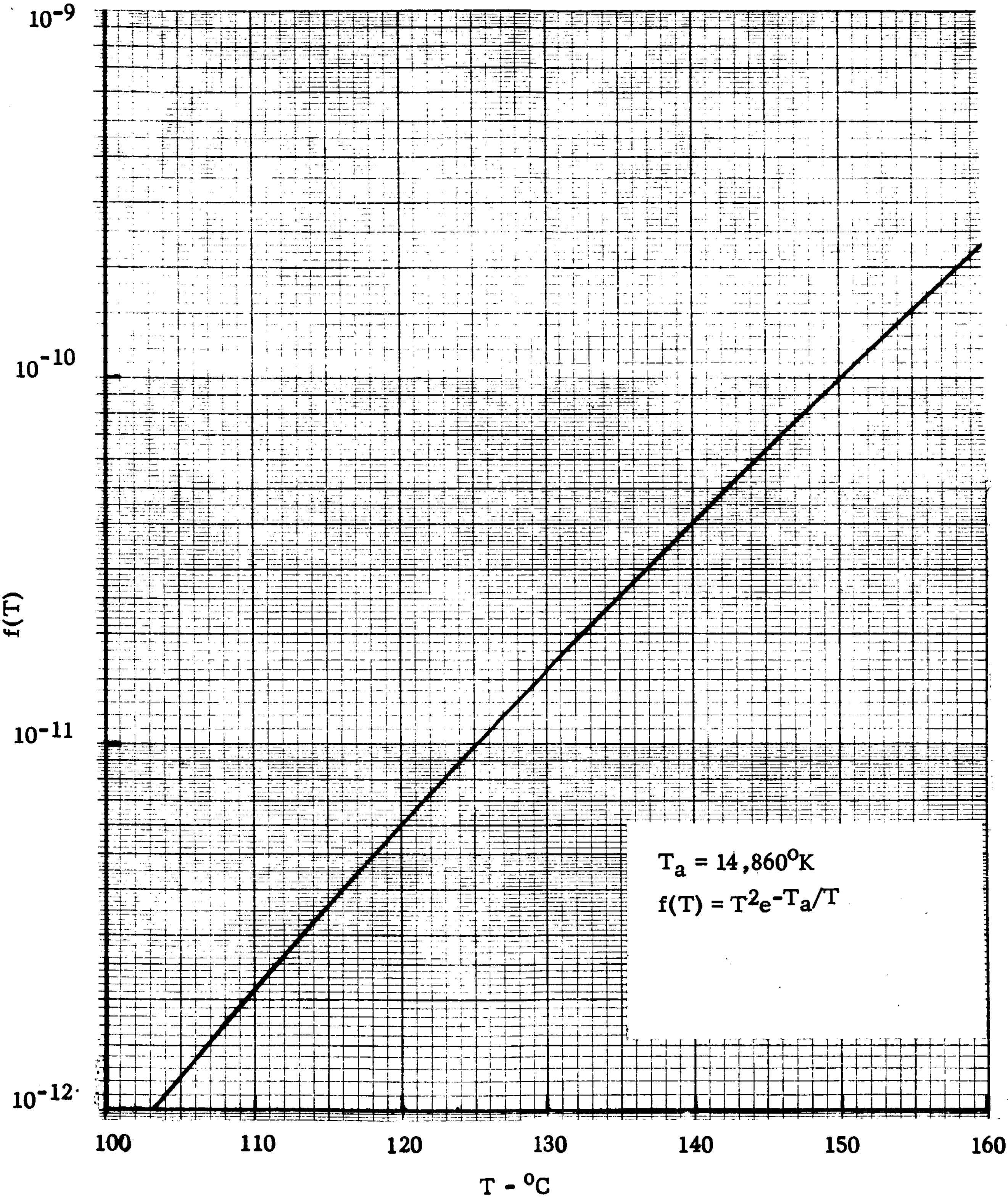


Figure A-1. Calculation Curve for Piece-Wise Integration of Sterilization Requirement Assuming Linear Temperature Change of integration. Since η can be viewed as the required number of decades of reduction in N_0, equation 18 gives the ratio of number of reduction decades achieved to the number of reduction decades required.

In the text, the results are expressed as percentages, i.e. the value of η calculated at the end of the transient heating period divided by the required value of $\eta = -12$, times 100. Thus a cumulative sterilization of, say, 150%, signifies that 18 decades of reduction have been achieved when only 12 are required.

APPENDIX B

Analysis of Transient Heat Transfer to a Sphere with Finite Surface Heat Transfer Coefficient

Consider a homogeneous sphere at uniform initial temperature T_i which, at time $\tau = 0$, is suddenly exposed to a furnace environment at a temperature of T^*. The solution for the temperature as a function of radius and time has been worked out by Heisler and reproduced in Jakob's book "Heat Transfer", Vol. I, pp. 284-291.

Following Jakob's presentation, we define:

T_o = temperature at center of sphere

θ_o = $(T^* - T_o)$

θ_i = $(T^* - T_i)$ = constant

T^* = environment (furnace) temperature

θ = $(T^* - T)$ = temperature at radius r and time τ (below furnace temperature)

T_s = surface temperature at r = s

θ_s = $(T^* - T_s)$

Heisler's charts present θ_o/θ_i and θ_s/θ_i as functions of bs and $\alpha\tau/s^2$ where

b = $\frac{h}{K}$

h = surface heat transfer coefficient

K = sphere thermal conductivity

α = $\frac{K}{\rho C_p}$ = thermal diffusivity

ρ = sphere density

C_p = sphere specific heat

s = sphere radius

τ = time

It can be shown that for bs = constant, a good approximation to Heisler's solution for values of $\alpha\tau/s^2$ greater than 0.2 is:

$$\log_{10} \frac{\theta_o}{\theta_i} = -C\left(\frac{\alpha\tau}{s^2}\right)$$

where C is a constant dependent only on the value of (1/bs).

In order to determine empirical values of K, ρ, and h which apply to a typical landing capsule, we use the experimental GE data (Ref. 1) for a small capsule which has the center heat up from 25°C to within 1°C of the furnace temperature of 150°C in 12 hours.

We assume that this capsule can be approximated as a sphere of 3 ft. diameter (s = 1.5 ft) with a density and effective thermal conductivity each one half that of solid aluminum. Then

$$\rho = 1/2(168) = 84 \text{ lb/ft}^3$$
$$K = 1/2(150) = 75 \text{ BTU/hr-ft}^\circ\text{F}.$$

We assume a surface heat transfer coefficient to the homogeneous sphere of

$$h = 4 \text{ BTU/hr-ft}^2\text{-}^\circ\text{F}.$$

Then

$$bs = \frac{hs}{K} = \frac{4(1.5)}{75} = 0.08$$

$$\frac{1}{bs} = 12.5$$

From Figures 13-17, page 287 of Jakob, we find

$$\frac{\theta_o}{\theta_i} = 0.5 \text{ for } \frac{\alpha\tau}{s^2} = 3 \text{ and } \frac{1}{bs} = 12.5$$

Therefore we find

$$C = \frac{-\log_{10}\frac{\theta_o}{\theta_i}}{\frac{\alpha\tau}{s^2}} = -\frac{\log_{10}(0.5)}{3} = \frac{0.3}{3} = 0.10$$

So $$\log_{10}\frac{\theta_o}{\theta_i} = -0.10\left(\frac{\alpha\tau}{s^2}\right)$$

Solving for the value of α required to make $\theta_o = 1^oC$ at $\tau = 12$ hours with $\theta_i = 150 - 25 = 125^oC$:

$$\alpha = \frac{s^2}{-0.10\,\tau} \log_{10} \frac{\theta_o}{\theta_i}$$

$$\alpha = \frac{1.5^2}{(-0.10)(12)} \log_{10} \frac{1}{125} = 3.93 \text{ ft}^2/\text{hr}$$

But since $\alpha = K/\rho C_p$

we find that with the above assumptions for K and ρ:

$$\alpha = \frac{75}{84(0.182)} = 4.9 \text{ ft}^2/\text{hr}.$$

Therefore the assumptions made above for K and ρ are not far from those needed to yield the empirically determined effective thermal diffusivity of $\alpha = 3.93$ ft^2/hr.

The central temperature T_o of the sphere then follows the equation:

$$\log_{10} \frac{(T^* - T_o)}{(T^* - T_i)} = -0.10 \frac{\alpha\,\tau}{s^2}$$

where
$$T_i = 25^oC$$
$$T^* = 150^oC$$
$$\alpha = 3.93 \text{ ft}^2/\text{hr}$$
$$s = 1.5 \text{ ft}.$$

or

$$T^* - T_o = (T^* - T_i)\, 10^{-\frac{0.10(3.93)}{1.5^2}\tau}$$

In degrees centigrade:

$$(150 - T_o) = (150 - 25)(10)^{-0.175\tau}$$

where τ is in hours.

This represents an exponential variation of temperature with time.

The curve of T_o vs. τ is given by the following tabular calculation:

τ (Hrs)	$10^{-.175\tau}$	$(150\text{-}T_0)$ (^oC)	T_0 (^oC)
0	1	125	25
4	0.25	31.2	118.8
6	0.0893	11.2	138.8
8	0.04	5	145
12	0.008	1	149

The plot of T_0 vs. τ is shown in Figure B-1 for comparison with the experimental GE data which was obtained with a furnace temperature increasing linearly with time for two hours. The idealized solution is plotted for two cases, one with a step-function change in furnace temperature at $\tau = 0$ and one with the change at $\tau = 2$ hrs. It is seen that if one assumes the step-function occurred at $\tau = 2$ hours, then the temperature-time curve from this simple theory is a fairly close approximation to the actual experimental data for the most thermally isolated component in the GE capsule experiment. It may be suspected that if the furnace had been programmed to heat up more rapidly, or if the capsule had been suddenly placed in a pre-heated furnace, this approximate exponential solution would be an even closer fit to the data.

In order to predict the behavior of a larger capsule, say a 10 ft. diameter sphere, we again assume:

$h = 4$ BTU/hr-ft^2-^oF

$K = 75$ BTU/hr-ft-^oF (1/2 that of Al)

$\alpha = 3.93$ ft^2/hr (as for small capsule)

Then

$$\frac{1}{bs} = \frac{K}{hs} = \frac{75}{4(5)} = 37.5$$

From Heisler's chart:

$$\log_{10}\left(\frac{\theta_o}{\theta_i}\right) = -C\left(\frac{\alpha\tau}{s^2}\right)$$

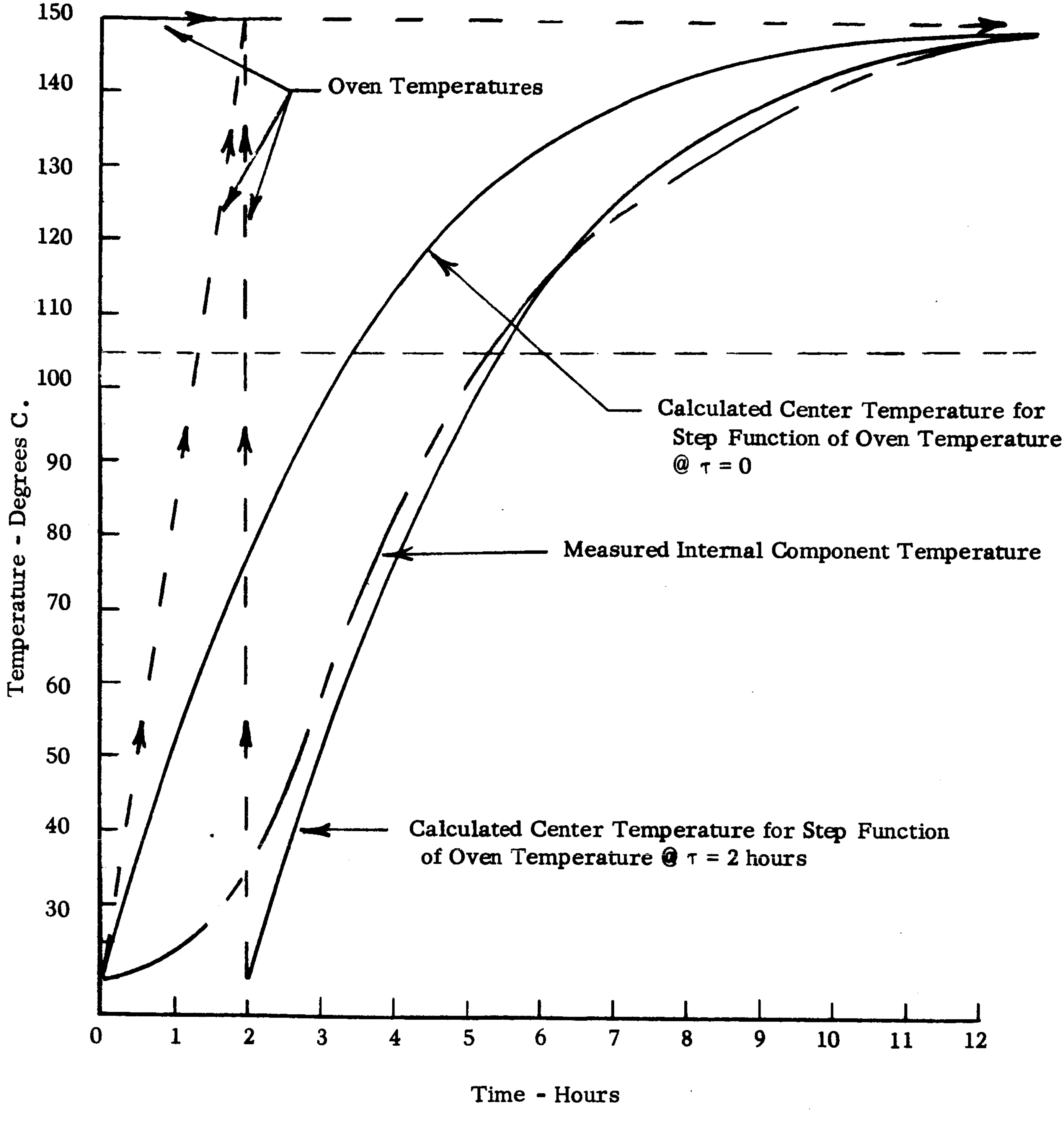


Figure B-1. Comparison of Calculated and Measured Internal Capsule Temperatures.

where for 1/bs = 37.5:

$$\frac{\theta_o}{\theta_i} = 10^{-2} \text{ for } \frac{\alpha\tau}{s^2} = 87$$

$$C = \frac{-\log_{10}(10^{-2})}{87} = \frac{2}{87} = 0.023$$

Then

$$\log_{10}\frac{(T^* - T_o)}{(T^* - T_i)} = \left[\frac{-0.023\alpha}{s^2}\right]\tau$$

$$= \frac{-0.023(3.93)}{(5)^2}\tau = -.00362\tau$$

Solving for the time required to heat the center of the sphere to within 1^oC of 150^oC:

$$\tau = \frac{\log_{10}\left(\frac{150-149}{150-25}\right)}{-0.00362}$$

$$\tau = \frac{\log_{10}(8 \times 10^{-3})}{-.00362} = \frac{-2.10}{-.00362} = 580 \text{ hrs.}$$

Therefore, unless some very effective internal heat transfer system were provided, a 10 ft sphere would require a prohibitively long heat-up time of 580 hours. The use of internal fans is one possible method for improving the effective thermal conductivity of a capsule.

APPENDIX C

Simplified Closed-Form Solution of Integrated Lethality during Spacecraft Heat-Up

We consider a planetary landing capsule which can be assumed to be a homogeneous sphere of radius s. Initially the capsule is at room temperature T_i and it is suddenly placed in an oven at a temperature T^*. We want to calculate the reduction in biological load at the center of the sphere due to the thermal exposure while the sphere heats up.

The analysis assuming an infinite heat transfer coefficient on the sphere surface has been reported by Jakob (Ref. 8, p. 264). The case of finite surface heat transfer coefficient has been solved by Groeber (Ref. 8, p. 281) and by Heisler (Ref. 8, p. 287). In all cases it can be shown that for times longer than about $s^2/2\alpha$ (where s is the sphere radius and α the thermal diffusivity) the central temperature T_o varies approximately exponentially with time according to:

$$\frac{T^* - T_o}{T^* - T_i} = e^{-t/\tau} \tag{1}$$

where τ = thermal time constant = $\frac{s^2}{\alpha}$.

To calculate bacterial lethality, we only consider the time after the sphere center temperature exceeds $T_{min} = 105^oC$ in accordance with sterilization requirements. Over a small temperature range, i.e. $105^oC \leq T \leq 125^oC$ the D-value for bacterial death can be approximated by: (Ref. 6)

$$\log D = \log D^* + Ky \tag{2}$$

where

D^* = D-value at furnace temp. T^*

K = constant

$y = \frac{T^* - T_o}{T^* - T_{min}}$ and $0 < y < 1$

The dimensionless ratio y is a measure of the amount by which the sphere center temperature is below the oven temperature.

It is assumed that the bacterial population decreases exponentially with time at a given temperature in accordance with:

$$\frac{d}{dt}\left(\log_{10}\frac{N}{N_o}\right) = -\frac{1}{D} \qquad (3)$$

where D is a function of temperature as given by equation 2. The logarithm of the population reduction ratio $R = N_o/N$ is given by:

$$\int_1^{\log_{10}R} d\left(\log_{10}\frac{N_o}{N}\right) = \int_o^t \frac{dt}{D} \qquad (4)$$

But from equation 1,

$$\frac{t}{\tau} = \ln\left[\frac{T^* - T_o}{T^* - T_i}\right] \qquad (5)$$

If we count time only from the time at which $T_o = T_{min} = 105^oC$, then

$$t = -\tau \ln\left[y\frac{(T^* - T_{min})}{(T^* - T_i)}\right] \qquad (6)$$

where

$$\frac{T^* - T_{min}}{T^* - T_i} = A = \text{constant.}$$

The differential form of equation 6 is

$$dt = -\tau\frac{dy}{y} \qquad (7)$$

which may be substituted in equation 4 to obtain

$$\log_{10}R = \int_{y=1}^{\epsilon} \frac{-\tau dy}{yD} \qquad (8)$$

where the upper limit of integration is given by $y = \epsilon$ and ϵ is a measure of the closeness of the center temperature to the oven temperature which is assumed to correspond to "steady state". For example, if $T^* = 125^oC$, $T_{min} = 105^oC$ and $\epsilon = 0.05$, then the final temperature differs from the oven temperature by

$$T^* - T_o = \epsilon\,(T^* - T_{min}) = .05(20) = 1^oC.$$

From equation 2

$$D = D^* e^{ky} \qquad (9)$$

which is substituted in equation 8 to get

$$\log_{10} R = \int_1^{\epsilon} \frac{-\tau\, dy}{D^* y e^{ky}} = \frac{\tau}{D^*} \int_{\epsilon}^{1} \frac{dy}{y e^{ky}} \qquad (10)$$

We now let $u = Ky \quad du = Kdy$.

Then

$$\log_{10} R = \frac{\tau}{D^*} \int_{\epsilon}^{1} \frac{du}{u e^{u}} \qquad (11)$$

This may be written in terms of the exponential integral

$$E_1(x) = \int_x^{\infty} \frac{du}{u e^{u}} \qquad (12)$$

So:

$$\log_{10} R = \frac{\tau}{D^*} \left[E_1(K\epsilon) - E_1(K) \right] \qquad (13)$$

This may also be written as

$$\log_{10} R = \frac{s^2}{\alpha D^*} \left[E_1(K\epsilon) - E_1(K) \right] \qquad (14)$$

where the thermal time constant has been replaced by the ratio s^2/α where s is the sphere radius and α the thermal diffusivity.

As an example, we assume:

$T^* = 125^{o}C$

$T_{min} = 105^{o}C$

$\epsilon = 0.05$

$D^* = 4.5$ hours

$K = 2.0$

The time constants are derived from data by GE with a small experimental capsule which has the following time constants, depending on the presence of a bio-canister and of a capsule fan:

Test	Canister	Capsule Fan	Time Constant τ
A-1	No	Yes	1.1 hr.
A-2	No	No	1.95 hrs.
A-3	Yes	No	3.5 hrs.

Equation 13 gives

$$\log_{10}R = \tau\left[\frac{E_1(0.10) - E_1(2.0)}{4.5}\right]$$

Referring to a table of exponential integrals (e.g. Etherington, "Nuclear Engineering Handbook", p. 1-120) we get:

$$\log_{10}R = 0.395\tau$$

which yields the following results for lethality during the heat-up period:

Test	τ	$\text{Log}_{10}R$
A-1	1.1	0.43
A-2	1.95	0.77
A-3	3.5	1.38

These results apply to a small capsule which can be approximated as an equivalent sphere having a radius of about 1.5 feet. Since τ varies as the square of sphere radius, the value of $\log_{10}R$ for larger capsules is shown in Figure C-1, assuming they have equivalent thermal diffusivity values as for the small capsule.

It is seen that for a sphere of 4.4 ft radius, the required load reduction of 12 D-values ($\log_{10}R=12$) would be achieved during the heat-up transient alone, assuming no holding at maximum temperature and neglecting the lethality during cool-down.

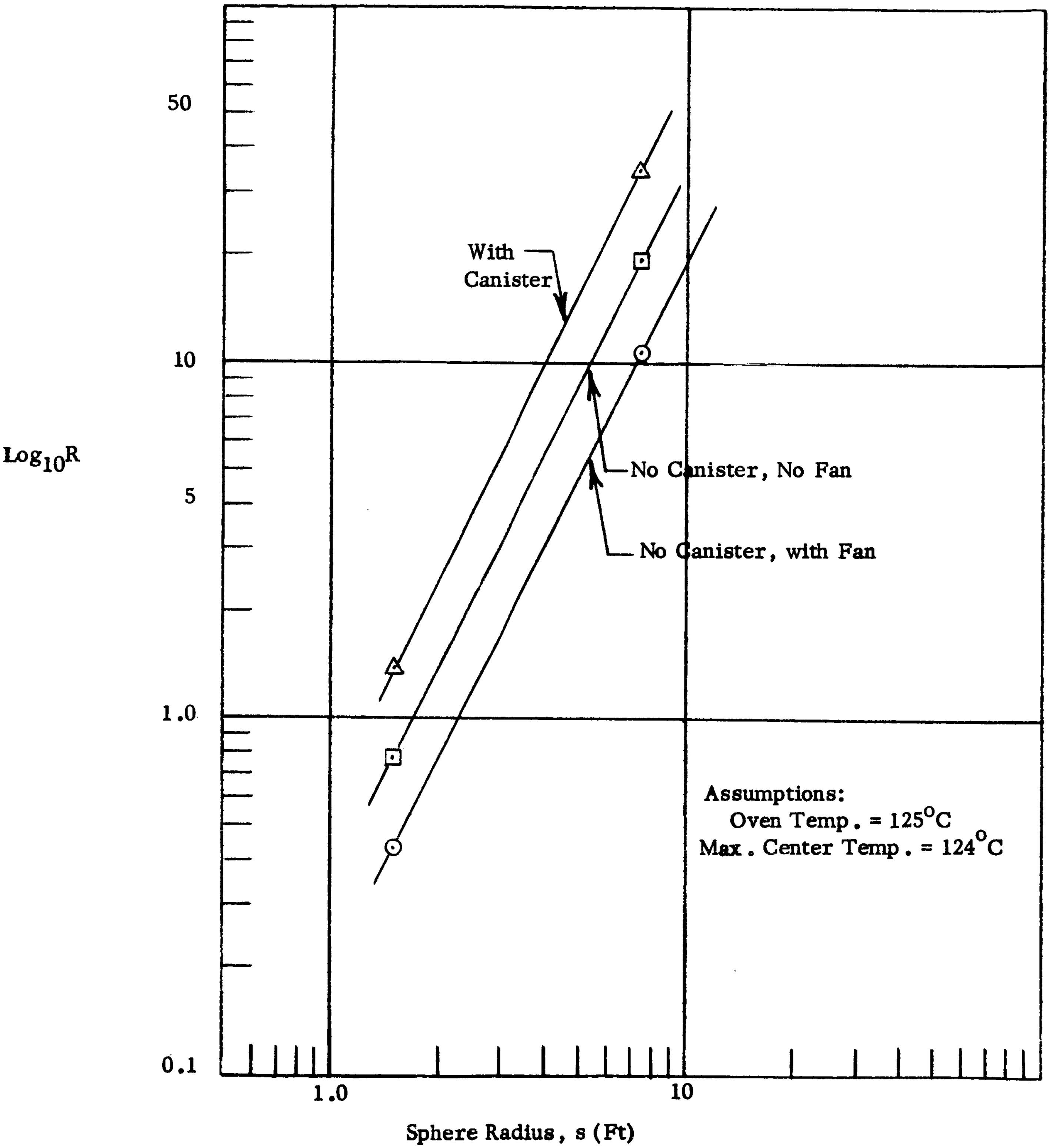


Figure C-1. Bacterial Reduction Ratio at Sphere Center Due to Heat-Up Transient Only

The lethality during cool-down has not been calculated because the variation of center temperature with time is more complicated than the simple exponential. Therefore, unless the equation is approximated by a relatively simple relationship, the lethality expression is not easily integrable.